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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	16

DATE MAILED: 02/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/674,254	Tabibzadeh
Examiner	**Art Unit**
Portner	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 13, 2002* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-13, 15-31, and 33-40* is/are pending in the application.

4a) Of the above, claim(s) *18* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-13, 15-17, 19-31, and 33-40* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-13, 15-31, and 33-40* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 14 and 32 have been canceled.

Claims 1-13,15-31,33-40 are pending.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restriction

2. Newly submitted claim 18 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 18 was previously directed to a method that "down regulating the expression of ebaf", but claim 18 has been amended to be directed to a method that comprises the step: "administering a compound" for down regulating the expression of ebaf. The compound is not limited to being a ebaf compound that would function to down regulate the expression, but is has been amended to recite a genus of methods that administer any type of compound that will down regulate expression. How, where or what the compound is, is claimed generically, and not so claimed to be specific for or to hybridize to ebaf. Claim 18 is directed to an invention that is independent and distinct from original claim 18, previously examined.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 18 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Rejections/Objections Withdrawn

3. This application now contains an abstract of the disclosure as required by 37 CFR 1.72(b).

4. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper inlight of the amendment of the specification to remove various notations that were unclear.

5. Claims 27-29 and 39 directed to antibodies and markers that are isolated and purified; the claimed invention is now directed to-statutory subject matter.
6. Claims 1-5, 9-14, 18-19, 22-26, 28-29,35, 37, 39-40 rejected under 35 U.S.C. 102(a) as being anticipated by Kothapalli et al (May 1997; different inventive entity), in light of the Declaration submitted with Applicant's amendment dated November 13, 2002.
7. Claims 1-3, 18-26 and 30 rejected under 35 U.S.C. 112, second paragraph for reciting methods steps in the passive voice.
8. Claim 1 rejected under 35 U.S.C. 112, second paragraph for reciting the term "ebaf".
9. Claim 2 rejected under 35 U.S.C. 112, second paragraph depends from claim 1 which recites "ebaf" and defines the screening step to further comprise either a Northern blot or a Western blot, in light of the amendment of claim 1 to recite the phrase "or the proteins encoded by ebaf".
10. Claim 3 rejected under 35 U.S.C. 112, second paragraph for reciting the phrase "further includes immunohistochemical staining", in light of the amendment of claim 1, from which claim 3 depends to recite tissue samples that could be immunohistochemically stained.
11. Claims 4-7 rejected under 35 U.S.C. 112, second paragraph, directed to a "screening means" in light of the means being disclosed in the instant specification.
12. Claim 8 rejected under 35 U.S.C. 112, second paragraph recites the phrase "ebaf protein", in light of claim 8 having been amended to recite the phrase "protein encoded by ebaf".
13. Claim 9 rejected under 35 U.S.C. 112, second paragraph for reciting the phrase "wherein the mRNA encoding ebaf is detected", in light of the amendment of claim 9 to recite the phrase "said screening means detects mRNA" and the means is limited to those means disclosed in the instant specification.
14. Claims 13 and 14 rejected under 35 U.S.C. 112, second paragraph, in light of the cancellation of claim 14.
15. Claim 15 rejected under 35 U.S.C. 112, second paragraph, in light of the sample being defined and the means being limited to those means defined in the instant specification.
16. Claim 16 rejected under 35 U.S.C. 112, second paragraph for reciting a "wherein" clause that defines "ebaf" to be a protein, in light of the claim having been amended to recite "a protein encoded by ebaf" .
17. Claims 28-29 rejected under 35 U.S.C. 112, second paragraph for reciting "a marker" for receptivity and infertility, both being defined to be ebaf, in light of Applicant's clarifying remarks.
18. Claim 31 rejected under 35 U.S.C. 112, second paragraph for reciting a "immunohistology test", in light of Applicant's clarifying remarks.
19. Claim 32 rejected under 35 U.S.C. 112, second paragraph for reciting the phrase "further includes antisera" and depends from claim 31, in light of claim 32 having been canceled.

Rejections/Objections Maintained

20. Claim 39 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record in paper number 13, paragraph 8.

21. Claims 1-13, 15-26, 28-31,33-38 and 40 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record in paper number 13, paragraph 9.

22. Claims 1-26,27, 28, 40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the utilization of serum and endometrial samples and antisera that specifically bind to EBAF for determining the presence or absence of EBAF in does not reasonably provide enablement for the determination of EBAF or variants thereof in any sample of tissue, or bodily fluid such as brain tissue, saliva, and fecal samples for the determination of fertility or infertility . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for reasons of record in paper number 13, paragraph 10, as the claims still recite samples of urine and saliva that would not predictably show levels of ebaf or EBAF, absent comparison to specific controls, specific reagents and obtained from a female at a specific time during the menstrual cycle, to diagnose, determine the prognosis of infertility, determine endometrial receptivity, in light of the prior art teaching other conditions such as, rectal, colon, kidney and pancreatic cancers produce increased levels of ebaf that would be present in the urine and saliva (bodily fluid) and would not directly correlate any level of ebaf or EBAF with female or male infertility or endometrial irregularities when compared with any control.

23. Claims 1-3 rejected under 35 U.S.C. 112, second paragraph for reciting the phrase "by screening" and not reciting the ebaf encoded protein, has been partially obviated, but claims 1-3 do not define any specific type of reference sample or control, any level of ebaf is set forth as being indicative of irregularities. The method does not define the urine or saliva sample to be

from a female and the level determined does not correlate with diagnosis. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

24. Claims 10-12 recite "wherein" clauses that define specific diseases that are diagnosed. What are the tools being claimed that will be used to diagnose these diseases? No specific tools are recited in the claims. Clarification of what is intended to be the tool, in light of the recitation of a disease being recited without any biological reagent with any specific structure or function being defined in the claims is requested. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

25. Claim 17 rejected under 35 U.S.C. 112, second paragraph defines because what components are in the diagnostic kit is not distinctly claimed (see claim 17 dependent upon claim 17). The rejection is maintained for reasons of record in paper number 13, paragraph 12.

26. Claim 18 rejected under 35 U.S.C. 112, second paragraph for reciting the phrase "by down-regulating the expression of ebaf"; claim 18 is incomplete, as essential reagents and methods steps are missing. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

27. Claim 19 rejected under 35 U.S.C. 112, second paragraph is directed to a method for "determining endometrial receptivity" has been partially obviated through amendment of the claim to recite specific types of samples, but the method does not provide a correlation step of any results determined with the recited preamble, and any level of ebaf would not determine endometrial receptivity, especially if the level of ebaf determined were indicative of an ovarian tumor (see US Pat. 5,916,751, evaluate blood samples.

28. Claims 20-23 rejected under 35 U.S.C. 112, second paragraph for reciting the same method as claim 19, with a different "by determining" phrase, has been partially obviated by amending the claims to recite specific types of samples, but no correlation methods steps defining what level of ebaf must be determined to correlate with the preamble of the claims has been set forth, nor have the urine or saliva samples been defined to be from a female. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

29. Claim 24-26 rejected under 35 U.S.C. 112, second paragraph for reciting the phrase "determining optimal treatment or treatment response", has been partially obviated by amending the claims to recite specific sample types, but the claims do not define the object that has received treatment, "optimal treatment", how treatment is achieved, what suboptimal treatment would be,

and what type of response to a treatment is being determined, nor have the levels determined been correlated with the preamble of the claim. The urine, serum or saliva samples have not been defined to have been obtained from a male or female animal. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

30. Claim 27 rejected under 35 U.S.C. 112, second paragraph, directed to an "antisera" "to ebaf", in light of the fact that an antisera specific to mRNA or DNA that encodes ebaf has been defined in the instant specification. This rejection could be obviated by amending the claim to recite --a protein encoded by human ebaf--. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

31. Claim 30 rejected under 35 U.S.C. 112, second paragraph for reciting the phrase "by modulating", in light of the claim not positively reciting what type of modulation of ebaf is being carried out to correlate with the preamble of the claim. No specific animal is recited in the claim, only ebaf is modulated, without a patient, fertility will not be modulated. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

32. Claim 33 rejected under 35 U.S.C. 112, second paragraph, for reciting a kit for an "immunoassay" defining the absence of antisera in the kit of claim 33, based upon the antisera being present in the kit of claim 34 which depends from claim 33. The reagents present in the kit of claim 33 are not distinctly claimed. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

33. Claims 34 and 36 rejected under 35 U.S.C. 112, second paragraph, for reciting the phrase "antisera and peptides as positive controls", wherein the binding specificity of the antisera and the specific structure and/or function of the peptides been defined to be ebaf or EBAF specific reagents and thus do not distinctly claim the a positive control. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

34. Claim 35 rejected under 35 U.S.C. 112, second paragraph, for reciting the phrase "blotting test", in light of what reagents and components are in the kit have not been distinctly claimed.The rejection is maintained for reasons of record in paper number 13, paragraph 12.

35. Claim 37-38 rejected under 35 U.S.C. 112, second paragraph, for reciting limitations directed to kits comprising "a PCR", Claim 38 comprises one or more probes, thus defining claim 37 not to comprise a detection reagent specific for ebaf. The invention is not distinctly claimed. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

36. Claim 40 rejected under 35 U.S.C. 112, second paragraph, for reciting claim limitations directed to a device for the detection of at least one variant of ebaf, but what the variant is, is not distinctly claimed, nor has the device been so claim to comprise a reagent to detect a variant of ebaf; the invention is not distinctly claimed.The rejection is maintained for reasons of record in paper number 13, paragraph 12.

37. Claims 4-12, 15-17, 27-29, 31-38, 40 rejected under 35 U.S.C. 102(e) as being anticipated by Tabibzadeh (US Pat. 6,294,662 (continuation of '751, priority back to August 1996') or US Pat. 5,916,751) for reasons of record in paper number 13, paragraph 15.

Response to Arguments

38. Applicant's arguments filed November 13, 2002 have been fully considered but they are not persuasive.

39. The rejection of claim 39 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is traversed on the grounds that "a variant is disclosed at page 27, lines 20-27. Various method of creating a variant and what would be included in the variant are disclosed."

40. The examiner upon reconsideration of the disclosure of the instant specification, especially page 27, lines 20-27 as pointed out by Applicant, the statement "By variant, it is meant that an variant which is functionally relevant" was found, but on specific functional variants or structural variants were found disclosed at this location in the specification. The claimed genus of peptides

which is argued to be able to be made, does not provide support for possession of the genus of variant peptides at the time of filing. The relevant function is not defined to be any specific function, but must only evidence a relative functional of being "relevant". What the relevant function is relative to, or relevant for, is not clear. The rejection is maintained for reasons of record in paper number 13, paragraph 8. This rejection could be obviated by amending the claim to recite : --An isolated and purified peptide consisting of CASDGALVPRRLQHRP-amide (SEQ ID NO 3).---

41. The rejection of claims 1-26, 28-38 and 40 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is traversed on the grounds that the examiner argued that the instant specification is "only discloses the nucleotide sequence for ebaf."

42. It is the position of the examiner that "The instant specification discloses the nucleotide sequence for ebaf, and "lefty" which is encoded by a sequence that share 77% sequence identity and 83% sequence similarity to ebaf, but a representative number of nucleotide sequences that would serve as detection reagents that could be used in methods, incorporated into devices, or diagnostic kits and are considered to be ebaf splice variants are described in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application."

43. Applicant traverses the rejection by pointing to page 20, line 20 through page 21, line 7 as support for variant forms of ebaf.

44. It is the position of the examiner that if Applicant intends the variants to be subportions of ebaf protein, based upon proteolytic cleavage of the preproprotein, then these fragments (discussion at page 20, line 20 through page 21, line 7 of the instant specification) should be recited in the claims relative to the disclosed preproprotein of the instant specification, but the instantly pending claims do not recite any specific nucleic acid means based upon structure correlated with function, nor do the claims recite a reagent defined by reference to a specific conserved sequence, nor are the nucleic acid molecules obtained from any specific source (ie human), bind to any specified sequence, hybridize to any specific sequence, nor stain in any specific pattern with a specific reagent. The instant claims are not so limited to the embodiment argued, but are directed to variant proteins, variant peptides and variant nucleic acid molecules, the sequences and functions of which are not claimed, nor disclosed in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application the genus of variants recited in the claims.

45. The rejection of claims 1-26,27, 28, 40 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the utilization of serum and endometrial samples and antisera that specifically bind to EBAF for determining the presence or absence of EBAF in does not reasonably provide enablement for the determination of EBAF or variants thereof in any

sample of tissue, or bodily fluid such as brain tissue, and fecal samples for the determination of fertility or infertility . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims is traversed on the grounds that "the utilization of antibodies is clearly disclosed on pages 24, line 29 through page 25, line 11; page 29, line 18 through page 31, line 14, and page 41,line 1 through page 42, line 6; and page 71,line 8 through page 72, line 15.

46. It is the position of the examiner that the instant specification teaches specific and non-specific antibodies that will immunoreact with any portion of EBAF peptide, which could and would cross react with other members of the TGFB family of proteins. Additionally, control antibodies are not defined to specifically immunoreact with peptides or proteins of EBAF (any portion thereof, see page 29, line 22), but may be any antibodies (page 29, lines 18-21), thus not defining a positive control for a specific diagnostic portion of EBAF. The claims still recite samples of urine and saliva that would not predictably show levels of ebaf or EBAF, absent comparison to specific controls, specific reagents and obtained from a female at a specific time during the menstrual cycle, to diagnose, determine the prognosis of infertility, determine endometrial receptivity, in light of the prior art teaching other conditions such as, rectal, colon, kidney and pancreatic cancers produce increased levels of ebaf that would be present in the urine and saliva (bodily fluid) and would not directly correlate any level of ebaf or EBAF with female or male infertility or endometrial irregularities when compared with any control.

No antibodies that immunoreact with ebaf (mRNA) are disclosed at any of the cited locations argued by Applicant; only antibodies directed to peptides and proteins of EBAF are described. While the specification clearly teaches specific reagents, the analysis of endometrial tissue, endometrium tissue extracts and serum samples, the specification does not teach the expression of ebaf in tissues that are not associated with fertility and infertility (reproductive tissues) and serum samples. Antisera to SEQ ID No 3 (a 16 amino acid peptide) is specific to EBAF and would be able to distinguish one member of the TGF-beta superfamily from another and specifically detect the presence or absence of EBAF.

None of the claims directed to methods, diagnostic tools, contraceptives, kits and devices recite any specific reagents of any specific binding specificities, of any specific structure and function, to comprise any specific amount of a reagent, nor any specific conditions for the determination of ebaf or EBAF correlated with the preamble of each method, or to have the recited ability to function as a contraceptive or diagnostic tool.

The instantly claimed invention is enabled for a scope of the claimed invention, as any antibody that does not specifically bind to a sequence of amino acids that is specific to EBAF, would not predictably detect or determine the presence of EBAF in a sample in light of the high level of shared amino acids sequences that EBAF has being a member of the TGF-B superfamily of molecules. The scope of enablement rejection is maintained for reasons of record in paper number 13, paragraph 10.

47. The rejection of claims 1-3 under 35 U.S.C. 112, second paragraph for reciting claims limitations that do not define any specific type of reference sample or control, any level of ebaf is set forth as being indicative of irregularities is traversed on the grounds that "the claims have been amended to more specifically recite the sample without prejudice."

48. It is the position of the examiner that the claimed methods of claims 1-3, do not define the urine or saliva sample to be from a female and the level of ebaf encoded protein or ebaf determined does not correlate with diagnosis. In light of the instant specification teaching that constitutive levels of ebaf and EBAF are produced by more than one tissue type, any level determined in endometrial tissue, urine or saliva would not be a diagnostic or prognostic level. The invention is not distinctly claimed. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

49. The rejection of claims 10-12 under 35 U.S.C. 112, second paragraph for reciting "wherein" clauses that define specific diseases that are diagnosed is traversed on the grounds that "the claims have been amended to recite that the diagnostic tool broadly claimed can be used in diagnosing multiple diseases" and asserts that "there is sufficient disclosure in the specification and sufficient clarity with regard to the language of the claims as presently pending.

50. It is the position of the examiner that the claimed "diagnostic tool" is not further defined through the recitation of several diseases. While the tool of claim 4 has been defined for analysis of specific samples, the tools being claimed in claims 10-12 which depend from claim 4, do not

evidence any specific structure or functions that differ from that of the tool of claim 4. Claims 10-13 seek to modify the preamble, the intended use of the tool and not the claimed tool. How a change of recited intended use of the claimed tool changes the diagnostic tool is not distinctly claimed. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

51. The rejection of claim 17 under 35 U.S.C. 112, second paragraph for not defining what components are in the diagnostic kit is not (see claim 17 dependent upon claim 17) traversed.

52. It is the position of the examiner that the rejection is maintained for reasons of record in paper number 13, paragraph 12, page 13, because what components are in the kit are not distinctly claimed.

53. The rejection of claim 18 rejected under 35 U.S.C. 112, second paragraph for reciting the phrase "by down-regulating the expression of ebaf" is traversed on the grounds that the specification discloses and enables any method of down regulating the expression of ebaf to be within the scope of the pending claim.

54. It is the position of the examiner that claim 18, though amended to recite the administration of a compound, is incomplete, as essential reagents and methods steps are missing. The claim has been with drawn from consideration as the nature and type of compound administered is not one that has been previously examined (election by original presentation). The rejection is maintained for reasons of record in paper number 13, paragraph 12.

55. The rejection of claim 19 rejected under 35 U.S.C. 112, second paragraph is traversed on the grounds that "the endometrial receptivity is for determining conception" and the determination is whether the endometrium is receptive to implantation and subsequent pregnancy".

56. It is the position of the examiner that the rejection under 35 U.S.C. 112, second paragraph has been partially obviated, but the method "determining endometrial receptivity" does not provide a correlation step of any results determined with the recited preamble, and any level of ebaf would not determine endometrial receptivity, especially if the level of ebaf determined were indicative of an other disease, specifically an ovarian tumor (see US Pat. 5,916,751). The saliva and urine samples are not obtained from a female, and the female samples are not taken at a time when ebaf levels would not be elevated (not during a female period). The claim still is missing essential methods steps and reagents, in order to distinctly claim Applicant's invention.

57. The rejection of claims 20-23 under 35 U.S.C. 112, second paragraph is traversed on the grounds that the methods are disclosed in the specification.

58. It is the position of the examiner that claims 20-23 do not recite a correlation methods steps defining what level of ebaf must be determined to correlate with the preamble of the claims, nor have the urine or saliva samples been defined to be from a female and the reagents have not been defined to be specific for the molecule being determined. Non-specific reagents are disclosed in the specification, as well as specific reagents; amendment of the claims to recite specific reagents

could partially obviate this rejection. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

59. The rejection of claim 24-26 under 35 U.S.C. 112, second paragraph is traversed on the grounds that the methods are disclosed in the specification.

60. It is the position of the examiner that the claims do not define the subject that has received treatment, how treatment is achieved, what suboptimal treatment would be, how any level of ebaf would be indicative of diagnosis or prognosis and what type of response to a treatment is being determined, nor have the levels determined been correlated with the preamble of the claim; nor have the urine, serum or saliva samples have not been defined to have been obtained from a male or female animal. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

61. The rejection of claim 27 rejected under 35 U.S.C. 112, second paragraph, is traversed on the grounds that the "antisera" "to ebaf" is disclosed at page 22, lines 22-31.

62. It is the position of the examiner that no antisera to a nucleic acid molecule "ebaf" have been disclosed, to include page 22, lines 22-31. This rejection could be obviated by amending the claim to recite --a protein encoded by human ebaf--. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

63. The rejection of claim 30 under 35 U.S.C. 112, second paragraph for reciting the phrase "by modulating", is traversed on the grounds that the specification teaches methods of modulation.

64. It is the position of the examiner that the claim does not positively recite what type of modulation of ebaf is being carried out to correlate with the preamble of the claim "regulate fertility". No compound is required to be administered. The human body of a female modulates ebaf expression based upon the normal hormonal cycle. The scope of the claim includes natural modulation by normal hormone cycling and in vitro modulation of ebaf, without a specific animal being recited in the claim, and a specific reagent being administered to a specific patient the invention is not distinctly claimed. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

65. The rejection of claim 33 under 35 U.S.C. 112, second paragraph, for reciting a kit for an "immunoassay" defining the absence of antisera in the kit of claim 33, based upon the antisera being present in the kit of claim 34 which depends from claim 33 is traversed on the grounds that the kits are defined at page 22, lines 20-31 of the specification.

66. It is the position of the examiner, upon reconsideration of page 22, lines 20-31, and the claim limitations recited in claim 33, relative to claim 34, the reagents present in the kit of claim 33 are not distinctly claimed. No specific immunological reagents are recited in claim 33. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

67. The rejection of claims 34 and 36 under 35 U.S.C. 112, second paragraph, for reciting the phrase "antisera and peptides as positive controls" is traversed on the grounds that the specification discloses sources and methods of creating antisera.

68. It is the position of the examiner that the specification discloses non-specific antibodies (see page 29, lines 18-21 and 22) that would not serve specifically detect or determine ebaf or EBAF, as well as antibodies to remove enzymes from a sample (see page 25, line 3) which would not serve to specifically determine, or diagnose EBAF or ebaf. The binding specificity of the antisera and the specific structure and/or function of the peptides have not been defined to be ebaf or EBAF specific reagents and thus do not distinctly claim a positive control. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

69. The rejection of claim 35 under 35 U.S.C. 112, second paragraph, for reciting the phrase "blotting test", is traversed on the grounds that the specification defines the components of the kit.

70. It is the position of the examiner that the reagents and components in the claimed kit have not been distinctly claimed. Kits are composition claims that contain any number of specific or non-specific reagents and are defined by the components contained therein. All kits to not contain the same reagents. The instantly claimed kits do not recite any reagents; the claim recite the phrase "for a blotting test". What is contained in the kit for the blotting test is not distinctly claimed. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

71. The rejection of claims 37-38 under 35 U.S.C. 112, second paragraph, for reciting limitations directed to kits comprising "a PCR"; Claim 38 comprises one or more probes, thus defining claim 37 not to comprise a detection reagent specific for ebaf is traversed on the grounds that the specification discloses the kits.

72. It is the position of the examiner that the reagents and components in the claimed kit have not been distinctly claimed. Kits are composition claims that contain any number of specific or non-specific reagents and are defined by the components contained therein. All kits to not contain the same reagents. The instantly claimed kits do not recite any reagents; the claims recite the phrase "a PCR". What is contained in the kit, of claim 37, for "a PCR" is not distinctly claimed. The rejection is maintained for reasons of record in paper number 13, paragraph 12.

73. The rejection of claim 40 under 35 U.S.C. 112, second paragraph, for reciting claim limitations directed to a device for the detection of at least one variant of ebaf, is traversed on the grounds that at page 27, lines 20-27 a variant is disclosed and at page 20, line 20 through page 21, line 7 variant forms of ebaf protein are disclosed and methods of distinguishing them are described.

74. It is the position of the examiner that the variant referred to at page 27, lines 20-27, though mentioned, has not been incorporated into a detection device. The disclosure at pages 20-21 discuss cleavage products of the 41 kDa preproprotein to be specific sizes of smaller pieces of the larger original protein, but the device of claim 40 is directed to variants of ebaf, the variant function and source of the variant are not recited in the claims, nor has the device been defined to

comprise any specific molecules or components that are specific for any type of variant ebaf molecule. The term "ebaf" is generally understood to mean a nucleic acid or gene designation, and not a protein. The device is not distinctly claimed.The rejection is maintained for reasons of record in paper number 13, paragraph 12.

75. The rejection of claims 4-12, 15-17, 20-21, 27-29, 31-38, 40 rejected under 35 U.S.C. 102(e) as being anticipated by Tabibzadeh (US Pat. 6,294,662 (continuation of '751, priority back to August 1996') or US Pat. 5,916,751), is traversed on the grounds that "there is no disclosure in the patent for the use of this in determining anything outside the scope of cancer."

76. It is the position of the examiner that kits are composition claims, with a recited intended use, the intended use of the claimed kits do not distinguish the kit from that disclosed in the prior art. No components of the instantly claimed kits define reagents specific for the intended method. The reagents, kits and devices of Tabibzadeh comprise the same or equivalent components of the instantly claimed invention(s). No reagents that distinguish the kits of the instant invention and that of Tabibzadeh have been claimed.

It was also noted that Tabibzadeh teaches the constitutive expression of ebaf gene is present in male and female tissues (see '662, col. 4,lines 55-58) which can be determined through the evaluation of a bodily fluid, teaches the endometrium tissue normally express levels of EBAF (see 6,294,662: col. 4, line 48) , and also teaches that increased levels of ebaf gene are expressed during a females period, and in a female that suffers from abnormal uterine bleeding (see '662:

col. 5, lines 1-5). Therefore, Tabibzadeh does disclose normal and abnormal levels of ebaf in a female that does and does not suffer from abnormal uterine bleeding (col. 4, lines 47-67 and col. 5, lines 1-5). Tabibzadeh provides disclosure with respect to female endometrium tissue, in addition to disclosure with respect to evaluation of sample for diagnosis of cancer. Tabibzadeh (US Pat 5,916,751) also teaches the same information at col. 4, lines 46 through col. 5, lines 1-4. The rejection is maintained for reasons of record in paper number 13, paragraph 15.

New Claim Limitations/New Grounds of Rejection

77. Claims 1-13, 15-16, 19-26, 28, and 40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Claims 1-13, 15-16, 19-26, 28, and 40 have been amended to recite the phrase "endometrial serum". The phrase lacks original descriptive support in the instant specification.

Upon consideration of the disclosure, the examiner found support for "endometrial fluid, serum, urine and saliva" at page 26, lines 1-3 and for "endometrium, endometrium fluid and placenta" at page 71, line 22, Example 5, but no original descriptive support could be found for "endometrial serum". Thus claims 1-13, 15-16, 19-26, 28, and 40 all recite New Matter.

The new matter should be removed in response to this office action. If original descriptive support is provided by the specification and was not noted by the examiner, Applicant

is invited to point out that portion of the specification from which this phrase "endometrial serum" finds original descriptive support.

Conclusion

78. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

79.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner

can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
February 4, 2003

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
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